

Chewell-Simer Lecture

Introductory ~~lecture~~ ^{remarks}.

"Some branch of physics of general interest."

What is molecular biology?

explaining anything biological in terms of physics & chemistry.

~~two roots~~ mainly gene-protein & their synthesis

but also muscle, nerve, etc.

two roots ① structural Astbury, Bernal.

② combination of ~~structure~~ biophysics, genetics, biochemistry, together with logical arguments

hence special name.

What is physics? "physics can explain everything,

chemistry & biology ~~are~~ included"

What do physicists actually know? ~~a little~~ ^{some} crystallography.

a little physical chemistry ~~and~~

hardly any organic chemistry

Board
over



DNA \rightsquigarrow RNA \rightsquigarrow protein

Nucleic Acid

Protein

poly polynucleotide chain

polypeptide chain

nucleotide

amino acid

phosphate - sugar - base

4 bases

20 side-chains.

genetic code

X-ray crystallography

Small molecules : & accurate bond distances and angles
rules for hydrogen bonding, etc.

the polypeptide chain _____ S
amino acid sequence + size
protein molecules : the phase problem.

the isomorphous replacement method.

number of reflections in reciprocal lattice.
(also photographic method) _____ S

Geiger counters : linear diffractometer _____ S
automatic collecting.

importance of computing
electron density maps. interpreting from _____ S
knowledge of structure.

plotting by computer _____ S

hard model of molecule _____ S

nucleic acid

DNA fibre diagrams _____ S

low resolution: screw axis (helical diffraction theory)

no many variables.

formulae of ΔN^2 _____ S

General nature of solution.

Structure of DNA _____ 3S

Example of a small molecule

a base pair in a crystal. _____ S
hydrogen bonds

electron microscope

~~depends~~ electrons can be detected by elastic or magnetic lenses.

Specimen must be in a vacuum. Thus dry: handicap for biological sp.

Limited penetration power.

Resolution limited by wavelength, λ and small aperture, due to spherical aberration, but down to 5-10 Å

main other limitation is due to contrast.

main methods

① Shading technique. gives a 3D impression.

| | | | |
|---------------------|---|------------|-----|
| classical technique | : | polyosomes | — S |
| modified technique | : | phage DNA | — S |

② Thin sections: with special microtome (diamond knife)

| | | | |
|----------|---|--|-----|
| examples | : | muscle: sarcomere, actin, myosin, sliding filaments | — S |
| some | : | cross-section | — S |
| staining | : | higher magnification org. | — S |

③ Negative contrast.

| | | | |
|--|--|--------------------|------|
| | | actin double helix | — S |
| | | TMV (+ model) | — 2S |
| | | Human wart virus | — 3 |

problem of one side v both sides. Klug's technique.

Radioactive tracers

very wide use: means one can study materials there
in small amounts. mainly ^{32}P , ^{14}C , ^3H : - automatic.

difficult to illustrate, because of the detailed

biochemistry.

example nearest neighbour analysis of DNA.

DNA replication by base pairing

can be done in test-tube. needs enzyme,

the 4 precursors and a template DNA.

method ————— S

results ————— S

autoradiography advantage of ^3H because of short range

show DNA in a horizontal cell ————— S

clears picture. emphasize the scale ————— S

Physical chemistry

briefly mention

① electrophoresis : free
paper
acrylamide gels.

example many abnormal human cells

② chromatography - paper
- ion exchange, etc.
- Sephadex.

③ ultracentrifuge - density,
sucrose gradient
density gradient.

example of density gradient Meselson-Stahl exp.

explain principle:

explain problem of DNA replication. ————— S

use of heavy ~~iso~~ isotopes ^{15}N to give density difference.

show result ————— S

explain "duplex"

fits in with idea of one long molecule, with a growing point.

Influence of people

Those who stayed outside

eg. Schrodinger "What is Life?"

the point of the book.

its influence.

Gamow idea of coding.

Those who came in

① the crystallographers. Arthur, Bernal, Bragg.

2nd generation [Penet, Kendrew - chemists!]

② those who do genetics of biochemists.

Max Delbrück - his school
his outlook.

Seymour Benzer.

Quite a number of others, mainly genetics bias.

Wally Gilbert and biochemistry.

Ideas

Two examples only.

① Symmetry : e.g. regular helix α -helix — S
also TMV rod virus.

and theory of spherical viruses.

icosahedron 60 subunits

almost-symmetrical structures — coiled coils — S

— actual virus structures.

? ?

② logic in genetics.

mutants of a special type

+ ad - — S

three plus mutant — S

conclude that a triplet code

(strictly a multiple of three).

Influence of physics

can be grouped under several headings.

① disciplines eg. (protein) crystallography.

② instruments and techniques eg. electron microscope
ultracentrifuge.

radioactive tracers.

③ ideas eg. simplicity.

Symmetry.

④ people either those who stayed as physicists
or those who gave up physics and
entered molecular biology.

Summing up.

Where would molecular biology be without physics?

modern physics (but not chemistry) was v. backward.

no crystallography

e/m

radioactive tracers

heavy isotopes.

and no physicists in biology.

more of molecular biology wiped out.

| | | |
|-------------|-----------------------|----------------------|
| but what if | no chemistry | } also important. |
| or | no physical chemistry | |
| or | no genetics | |

but then could be another lecture!